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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,741	11/14/2005	Hiroyuki Aburatani	392.1001	4248

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,741	ABURATANI ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11-13 and 19-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,12,13, 19,21, 22* is/are rejected.

7)☒ Claim(s) *11 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/28/06;6/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed December 14, 2006 in response to the Office Action of June 14, 2006, is acknowledged and has been entered. Previously pending claims 8, 10 and 14-16 have been cancelled, claims 9 and 11-13 have been amended and new claims 19-22 have been added.

2. Claims 9, 11-13, and 19-22 are currently being examined.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. It is noted that the amendment of claim 9 to "an isolated antibody" overcomes the rejection of claim 9, 11, and 13 under 35 USC 101. Applicant did not specifically point to support for the amendment to "an isolated antibody", but a review of the application by the Examiner found support for the isolated antibody to the C-terminal peptide of GPC 3 of claim 9 on page 26, the 1st full paragraph and pages 7-9, to which the paragraph on p. 26 refers.

Declaration of Inventor Iwao Ohizumi Under 37 CFR 1.132

5. It is noted for applicant's convenience that although the MPEP provides a mechanism to remove authors from a prior art publication for art purposes by filing an affidavit or declaration under 37 CFR 1.131, see MPEP 701 (c) below:

> Where the applicant is one of the co-authors of a publication cited against his or her application, he or she may overcome the rejection by filing an affidavit or declaration under 37 CFR 1.131. Alternatively, the applicant may overcome the rejection by filing a specific affidavit or declaration under 37 CFR 1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. 102(a). In re Katz, 687 F.2d 450, 215 USPQ 14 (CCPA 1982).

Removal of inventors from a patent application requires as follows:

1.48 Correction of inventorship in a patent application, other than a reissue

application, pursuant to 35 U.S.C. 116.
(a) Nonprovisional application after oath /declaration filed . If the inventive entity is set forth in error in an executed § 1.63 oath or declaration in a nonprovisional application, and such error arose without any deceptive intention on the part of the person named as an inventor in error or on the part of the person who through error was not named as an inventor, the inventorship of the nonprovisional application may be amended to name only the actual inventor or inventors. Amendment of the inventorship requires:
(1) A request to correct the inventorship that sets forth the desired inventorship change;
(2) A statement from each person being added as an inventor and from each person being deleted as an inventor that the error in inventorship occurred without deceptive intention on his or her part;
(3) An oath or declaration by the actual inventor or inventors as required by § 1.63 or as permitted by §§ 1.42, 1.43 or § 1.47;
(4) The processing fee set forth in § 1.17(i); and
(5) If an assignment has been executed by any of the original named inventors, the written consent of the assignee (see § 3.73(b) of this chapter).
(b) Nonprovisional application —fewer inventors due to amendment or cancellation of claims . If the correct inventors are named in a nonprovisional application, and the prosecution of the nonprovisional application results in the amendment or cancellation of claims so that fewer than all of the currently named inventors are the actual inventors of the invention being claimed in the nonprovisional application, an amendment must be filed requesting deletion of the name or names of the person or persons who are not inventors of the invention being claimed. Amendment of the inventorship requires:
(1) A request, signed by a party set forth in § 1.33(b), to correct the inventorship that identifies the named inventor or inventors being deleted and acknowledges that the inventor's invention is no longer being claimed in the nonprovisional application; and
(2) The processing fee set forth in § 1.17(i).
(c) Nonprovisional application —inventors added for claims to previously unclaimed subject matter . If a nonprovisional application discloses unclaimed subject matter by an inventor or inventors not named in the application, the application may be amended to add claims to the subject matter and name the correct inventors for the application. Amendment of the inventorship requires:
(1) A request to correct the inventorship that sets forth the desired inventorship change;
(2) A statement from each person being added as an inventor that the addition is necessitated by amendment of the claims and that the inventorship error occurred without deceptive intention on his or her part;
(3) An oath or declaration by the actual inventors as required by § 1.63 or as permitted by §§ 1.42, 1.43, or § 1.47;
(4) The processing fee set forth in § 1.17(i); and

(5) If an assignment has been executed by any of the original named inventors, the written consent of the assignee (see § 3.73(b) of this chapter).

Declarant Ohizumi states that he, and not the declared inventors of US patent application 10/481,524, is the inventor of the subject matter claimed in the application. It appears, given that each inventor that signs the declaration is required to have invented the claimed subject matter, that inventor Ohizumi is alerting the office to a fraudulent patent application. Clarification is required.

6. The following rejections are being maintained:

Claim Rejections - 35 USC 112

7. Claim 12 remains rejected under 35 USC 112 second paragraph for the reasons previously set forth in sections 9 of the Office Action of June 14, 2006, pages 3-4.

Applicants argues that that the definition of the term "chimera antibody" is specifically described in the specification at page 19, lines 3-9, and those skilled in the art can easily understand the structure of the chimeric antibody from the disclosure of the specification.

This argument has been considered, but has not been found persuasive because a review of the specification at page 19, lines 3-9 revealed the following non-limiting definition of chimera antibody:

> Chimera antibody can be obtained by linking the DNA encoding the V region of the antibody as obtained in the manner described above to DNA encoding the C region of a human antibody, inserting the resulting DNA in an expression vector, and introducing the vector in a host for production of the antibody. Using this existing method, a chimera antibody useful in accordance with the invention can be obtained.

This description of a chimeric antibody is only a description of what a chimera antibody can be and is not limiting. Thus, it does not provide an explicit description of what chimera antibody is

and the metes and bounds of the claims cannot be determined using the above teaching of the specification.

Applicants argue that a submitted copy of several pages from a common textbook published before the priority date of this application explicitly sets forth the meaning of the term "chimeric antibody" (see Clinical Aspects of Immunology, Blackwell Scientific Publications 5th Edition, 1993, pp. 823-24). Applicants argue that this textbook demonstrates that those skilled in the art could recognize the meaning of the term as of the priority date of the present application.

This argument has been considered, but has not been found persuasive because Clinical Aspects of Immunology teaches that even for "simple" chimeric antibodies a variety of antibodies have been made with constant regions of different species (see p 823, left col.). Clinical Aspects of Immunology also teaches the other forms of antibody fusions such as enzyme antibody fusions (see p. 823, left column) and reshaped antibodies (see p. 824, right column) that would be encompassed by the term chimera antibody as discussed in the rejection of claim 12 in sections 9 of the Office Action of June 14, 2006, pages 3-4. The reference supports Examiner's argument that the term chimera is generic to a class of antibodies, which are products of genetic shuffling of antibody domain and other active proteins. Thus, in the absence of a limiting definition of chimera antibody, claim 12 remains indefinite.

7. Claim 13 remains rejected under 35 USC 112 first paragraph for the reasons previously set forth in sections 13 and 14 of the Office Action of June 14, 2006, pages 10-17.

Applicant argues that according to the Examiner the specification is enabled for a cytotoxic, anticancer agent, comprising an antibody to SEQ ID NO: 4 amino acid residues 359-380 and 375-580, but not for cytotoxic, anti-cancer agent to the C-terminal peptide of GPC3.

Applicant argues that amendment of claim 9 to using the "consisting of" claim language and the change in dependency of claim 13 to depending on claim 9 satisfies the enablement requirement

Applicant's arguments have been carefully considered, but not been found persuasive and the rejection is maintained. Applicant appears to be referring to the rejection in section 14) when Applicant states that according to the Examiner the specification is enabled for a cytotoxic, anticancer agent, comprising an antibody to SEQ ID NO: 4 amino acid residues 359-380 and 375-580. This statement is based on Applicant being able to overcome the rejection of claim 13 in section 13) under 35 USC 112 first paragraph, which Applicant has not directly addressed or overcome.

Although the isolated antibody is now drawn to an isolated antibody against a C-terminal peptide of GPC3, wherein the C-terminal peptide of GPC3 is a peptide consisting of amino acid residues 359-580 of GPC 3 or a peptide consisting of amino acid residues 375-580 of GPC3, as set forth in SEQ ID NO: 4, this does not overcome the unpredictability of the contemplated use of the cytotoxic antibody for cancer therapeutics as described by Gura on p. 12 in the Office Action of June 14, 2006. The amendments also do not address the difficulties of treating solid tumors described by Jain on page 13 in the Office Action of June 14, 2006, nor do they address the limited success of cancer therapeutics and the difficulty of drug delivery discussed by Curti on page 13 in the Office Action of June 14, 2006. As noted on p. 15 of the Office Action of June 14, 2006, the specification teaches that chimeric monoclonal antibodies, ch. M3C11 and ch. M1E07, to the C-terminal peptide of amino acid residues 359-580/375-580 were shown to effectively mediate antibody dependent cellular cytotoxicity (p. 64, 2nd para.) and compliment dependent cytotoxic activity (p.67, 2nd para.) in ***in vitro*** assays using cell lines. The specification

speculates that if said antibodies are used for treating hepatoma, the antibodies can efficiently reach hepatoma cells without being trapped by the secreted form of GPC3, the N-terminal peptide, present in blood. The specification speculates that, thus, such antibodies are useful as agents for disrupting cancer cells and as anticancer agents (p. 68, 2nd para.). However, the specification provides no evidence that these cytotoxic antibodies can predictability be used for cancer therapies for the reasons set forth previously and above. Thus, the rejection of claim 13 is maintained.

New Grounds of Rejections

8. Claims 21 and 22 are rejected under 35 USC 112 first paragraph for the reasons set forth above for claim 13.

9. Claims 9 and 19 are rejected under 35 U.S.C. 102(b) as being as being anticipated by Huber (PhD Dissertation, Washington University, published December 1998, cited previously).

The claims are drawn to an isolated antibody against a C-terminal peptide of GPC3, wherein the C-terminal peptide of GPC3 is a peptide consisting of amino acid residues 359-580 of GPC 3 or a peptide consisting of amino acid residues 375-580 of GPC3, as set forth in SEQ ID NO: 4 (Claim 9) and the antibody claimed in claim 9 which is a recombinant antibody (Claim 19).

Huber teaches two anti-GPC3 polyclonal antibodies (para. bridging p. 151 and 152). Given that the antibodies are polyclonal antibodies, it would be expected that at least a subset of the polyclonal antibodies would bind to the C-terminal peptide of GPC3.

Although Huber does not specifically teach that the polyclonal antibodies bind to residues 359-580 and/or 375-580 of GPC 3 as set forth in SEQ ID NO: 4, it would be expected that at

least a subset of theses polyclonal antibodies would bind to said C-terminal portions of GPC3. Thus, absent a showing of unobvious differences, the polyclonal antibody that binds to GPC3 taught by Huber appears to be the same as of the instant invention. Since the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977) and Ex Parte Gray 10 USPQ 2nd 1922 (PTO Bd, Pat. App & Int, 1989).

Furthermore, given that all antibodies are recombinant, i.e. they are made by the recombining of different protein elements to form the different regions of the antibody (i. e., the antigen binding region, the Fc region, the heavy and light chain) the product of the prior art comprises the same product as claimed in the instant invention, that is, a recombinant antibody against a C-terminal peptide of GPC3, thus the claimed product is anticipated because the product will inherently be a recombinant antibody against the C-terminal peptide of GPC3. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the antibodies were recombinant antibodies, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art

and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

10. Claims 9, 13, 19, 21, and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Aburatani et al. (U. S. Pat. App. No: 10/481,524, Pub No.: US2004/0236080 A1, June 21, 2002, A1, cited previously).

The claims are drawn to an isolated antibody against a C-terminal peptide of GPC3, wherein the C-terminal peptide of GPC3 is a peptide consisting of amino acid residues 359-580 of GPC 3 or a peptide consisting of amino acid residues 375-580 of GPC3, as set forth in SEQ ID NO: 4 (Claim 9); the antibody claimed in claim 9 which is a cytotoxic antibody (Claim 13); the antibody claimed in claim 9 which is a recombinant antibody (Claim 19); the antibody claimed in claim 13 wherein the cytotoxic antibody has ADCC activity (Claim 21); and the antibody claimed in claim 13 wherein the cytotoxic antibody has CDC activity (Claim 22).

Aburatani et al. teach the anti-glypican 3 antibody used in the present invention can be obtained by a known means as a polyclonal or a monoclonal antibody, see para 0028 of the published application. Aburatani et al. teach that the antibodies of the invention can be isolated from the cells or host animals, and purified to a uniform level, see para 0083 of the published application. Aburatani et al. teach that the antibodies used in the present invention have ADCC activity or CDC activity as cytotoxic activity, see para 0089 of the published application.

Although Aburatani et al. does not specifically teach that the polyclonal antibodies bind to residues 359-580 and/or 375-580 of GPC 3 as set forth in SEQ ID NO: 4, it would be expected that at least a subset of these polyclonal antibodies would bind to said C-terminal portions of GPC3. Thus, absent a showing of unobvious differences, the polyclonal antibodies

that bind to GPC3 taught by Aburatani et al. appears to be the same as of the instant invention. Since the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977) and Ex Parte Gray 10 USPQ 2nd 1922 (PTO Bd, Pat. App & Int, 1989).

Furthermore, given that all antibodies are recombinant, i.e. they are made by the recombining of different protein elements to form the different regions of the antibody (i. e., the antigen binding region, the Fc region, the heavy and light chain) the product of the prior art comprises the same product as claimed in the instant invention, that is, a recombinant antibody against a C-terminal peptide of GPC3, thus the claimed product is anticipated because the product will inherently be a recombinant antibody against the C-terminal peptide of GPC3. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the antibodies were recombinant antibodies, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

10. Claims 11 and 20 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. No claim is allowed.

12. All other objections and rejections recited in the Office Action of June 14, 2006 are withdrawn.

13. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice

of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

13. Applicant's amendments necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0890. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR

SUSAN UNGAR, PH.D
PRIMARY EXAMINER